

B1
Cont

amino acid sequence containing the N-terminal in SEQ ID NO:3 and its homologous amino acid sequences. Variants, which have homologous amino acid sequence to the one in SEQ ID NO:3, can be obtained by replacing one or more amino acids in SEQ ID NO:3 with other amino acids without alternating the inherent biological properties of the present protein. Even when used the same DNA and depending on hosts into which the DNA is introduced, as well as on the components of nutrient culture media, the conditions of cultivation temperature and pH for culturing transformants containing the DNA, it may be formed variants, which are defective in or additionally contain one or more amino acids near to the N-terminal in SEQ ID NO:3 while retaining the inherent biological properties of the protein, by the modification with internal enzymes of the hosts after the DNA expression. The present protein includes such variants as long as they induce the IFN- γ production by immunocompetent cells.

IN THE CLAIMS

Please replace claims 1-8 with new rewritten claims 1-8 as follows below. A marked up version of the amended claims to show the changes made is attached hereto.

B2 *del c2*

1 (Once-amended). An IFN- γ production inducing agent which consists essentially of an effective ingredient capable of inducing IFN- γ production by immunocompetent cells, said effective

ingredient consisting of a protein (IGIF, IL-18) having the following physicochemical properties:

- (1) Molecular weight
19,000±5,000 daltons on gel filtration and sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE);
- (2) Isoelectric point (pI)
4.8 ± 1.0 on chromatofocusing;
- (3) Biological activity
Inducing the interferon- γ production by immunocompetent cells; and
- (4) Partial amino acid sequence
Possessing a part or the whole of the amino acid sequence of SEQ ID NO:2, wherein Xaa is Met or Thr.

2(Once-amended). A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and an effective ingredient capable of inducing IFN- γ production by immunocompetent cells, said effective ingredient consisting of a protein (IGIF, IL-18) having the following physicochemical properties:

- (1) Molecular weight
19,000±5,000 daltons on gel filtration and sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE);
- (2) Isoelectric point (pI)

4.8 \pm 1.0 on chromatofocusing;

(3) Biological activity

Inducing the interferon- γ production by immunocompetent cells; and

(4) Partial amino acid sequence

Possessing a part or the whole of the amino acid sequence of SEQ ID NO:2, wherein Xaa is Met or Thr.

3(Once-amended). A purified protein which is a variant of a protein (IGIF, IL-18) having the following physicochemical properties:

(1) Molecular weight

19,000 \pm 5,000 daltons on gel filtration and sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE);

(2) Isoelectric point (pI)

4.8 \pm 1.0 on chromatofocusing;

(3) Biological activity

Inducing the interferon- γ production by immunocompetent cells; and

(4) Partial amino acid sequence

Possessing a part or the whole of the amino acid

sequence of SEQ ID NO:2, wherein Xaa is Met or Thr,

wherein said variant has the amino acid sequence of SEQ ID NO:2

with at least one amino acid residue in SEQ ID NO:2

replaced with different amino acid or at least one amino acid residue deleted or added to the N-terminus of SEQ ID NO:2 while not substantially altering the physicochemical properties of the protein.

4(Once-amended). The purified protein according to claim 3, wherein said variant has at least one amino acid residue in SEQ ID NO:2 replaced with a different amino acid residue.

5(Once-amended). The purified protein according to claim 3, wherein said variant has at least one amino acid residue deleted or added to the N-terminus of SEQ ID NO:2.

6(Once-amended). A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and, as an active ingredient, the protein of claim 3.

B2
cont *See C3* 7(Once-amended). A purified protein (IGIF, IL-18) which has the amino acid sequence of SEQ ID NO:2, where Xaa represents methionine or threonine.

8(Once-amended). An IFN- γ production inducing agent which consists essentially of, as an effective ingredient, the protein of claim 7.

Please cancel claim 10 without prejudice and add new claims 11-15 in place thereof as follows:

B3 *See C4* 11. A purified protein (IGIF, IL-18), which has the following physicochemical properties:

- (1) Molecular weight
19,000±5,000 daltons on gel filtration and sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE);
- (2) Isoelectric point (pI)
4.8 ± 1.0 on chromatofocusing;
- (3) Biological activity
Inducing the interferon- γ production by immunocompetent cells; and
- (4) Partial amino acid sequence
Possessing a part or the whole of the amino acid sequence of SEQ ID NO:2, wherein Xaa is Met or Thr, and which reacts with a monoclonal antibody specific to a protein or a variant of the protein having the amino acid sequence of SEQ ID NO:2 with at least one amino acid residue in SEQ ID NO:2 replaced with a different amino acid, or at least one amino acid residue deleted or added to the N-terminus of SEQ ID NO:2, while not substantially altering the physicochemical properties of the protein.--

--12. An isolated protein of IGIF (IL-18).--